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CASE REPORT
Reconstructive

# Histopathologic Analysis of a Recalcitrant Calcaneal Wound Treated Using a Synthetic Hybrid-scale Fiber Matrix

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**Summary:** Traditionally, full-thickness wounds with exposed structures are treated with flap coverage or dermal regenerative templates. Most dermal regenerative templates are biologic in origin, but recently synthetic options have become available. One such product is a synthetic hybrid-scale fiber matrix (SHSFM). In this case, SHSFM was used to treat a recalcitrant calcaneal wound. After the wound granulated, it was biopsied, and histopathologic analysis was conducted. A 16-year-old woman involved in a motor vehicle collision sustained multiple traumatic injuries which were stabilized. Postoperatively, she developed a calcaneal infection and associated wound, which developed into a chronic, nonhealing wound. Failed treatments included removal of hardware, multiple debridements, and advanced wound therapies. An SHSFM was then trialed, which led to granulation of the wound without infection. Despite wound healing, the patient subsequently elected to undergo a below-the-knee amputation due to pain and functional disability from posttraumatic ankle arthritis. The heel was biopsied at the time of amputation for analysis. Pathologists noted excellent granulation tissue formation and complete coverage of the wound surface area and 75% of the wound depth, which included epithelialization and decreasing inflammation at wound edges. Collagen deposition and numerous interspersed blood vessels were present. Foreign material and bacteria were absent. No osteomyelitis was observed. This analysis provided the opportunity to investigate the in vivo regenerate from a novel synthetic SHSFM. Given the uniqueness and challenges presented in this case, the usage of this relatively new product warrants further investigation with larger populations and assorted wound etiologies. *(Plast Reconstr Surg Glob Open 2024; 12:e5597; doi: 10.1097/GOX.0000000000005597; Published online 6 February 2024.)*

Soft tissue trauma reconstruction can be complex and may result in tissue necrosis and infection. Flaps provide coverage over large defects but may not be appropriate depending on patient comorbidities or infection risk.[1,2] Dermal regenerative templates may also be considered to facilitate cellular migration and accelerate healing.[3,4]

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A synthetic hybrid-scale fiber matrix (SHSFM) (Restrata, Acera Surgical, Inc., St. Louis, Mo.) provides a synthetic, electrospun, polymer matrix that resembles extracellular matrix (ECM) to support cellular ingrowth. The SHSFM resorbs via hydrolysis at an engineered rate matching tissue ingrowth, increasing matrix porosity and supporting natural wound healing processes.[5]

Preclinical studies of SHSFM in full-thickness swine wounds demonstrated less inflammation, increased granulation tissue formation, and more mature collagen deposition compared with a bilayer xenograft matrix.[6] Histopathologic assessment of hematoxylin and eosin (H&E) stained slides was conducted in a manner consistent with International Organization for Standardization 10993-6 semiqualitative standards.[6]

In this report, a SHSFM-treated calcaneal wound was processed into H&E-stained slides for semiqualitative pathologist assessment. This clinical case provided an opportunity for histopathologic assessment of the

Disclosure statements are at the end of this article, following the correspondence information.

SHSFM's effect on human tissue for the first time and to determine if positive preclinical results translate to real-world clinical settings.

## METHODS

A 16-year-old girl involved in a motor vehicle collision underwent treatment of multiple fractures, including open reduction, internal fixation and multiple free flap coverage of an open pilon, and open reduction, internal fixation of a closed calcaneus fracture on the ipsilateral limb. Postoperatively, she developed a calcaneal infection and associated wound with retained hardware, which was initially treated with antibiotics and debridement and subsequently healed. Due to retained hardware, the infection recurred. After hardware removal and debridement, a large heel wound with exposed, periosteum-devoid bone remained. At its largest, the wound measured 10.0 cm × 6.0 cm × 3.5 cm. Given concerns of donor site morbidity with a history of poor wound healing, wound location, and weightbearing status, the patient declined another flap. A partial calcanectomy with intrawound and IV antibiotics as well as vac therapy was completed. Subsequent treatments with urinary bladder matrix, vac therapy, and antibiotics were trialed without success (Fig. 1).

The patient was educated on the SHSFM and agreed to treatment. The SHSFM was applied 12 times over 7 months. At each application, the wound was debrided; the SHSFM was cut to size, applied, and covered with a nonadherent dressing; and a wound vac was placed. Halfway through treatment the wound measured 7 cm × 7 cm × 1 cm, warranting continuation of application. Reapplication was performed after resorption of the prior application. This led to granulation of the wound without infection (Fig. 2). At the last application, the wound was 6.25 cm × 5.0 cm × 1.0 cm and sufficiently prepared for skin-grafting. Unfortunately, the patient reported severe pain and functional disability due to posttraumatic ankle arthritis. After consultation with a reconstructive foot and ankle specialist, the patient elected to undergo a below-the-knee amputation 10 months after SHSFM application, 3.5 years after initial injury.

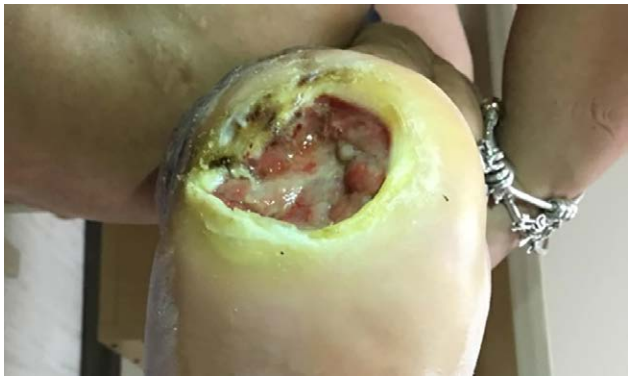

**Fig. 1.** Calcaneal wound with exposure of devitalized bone 1 month before initial application of the SHSFM.

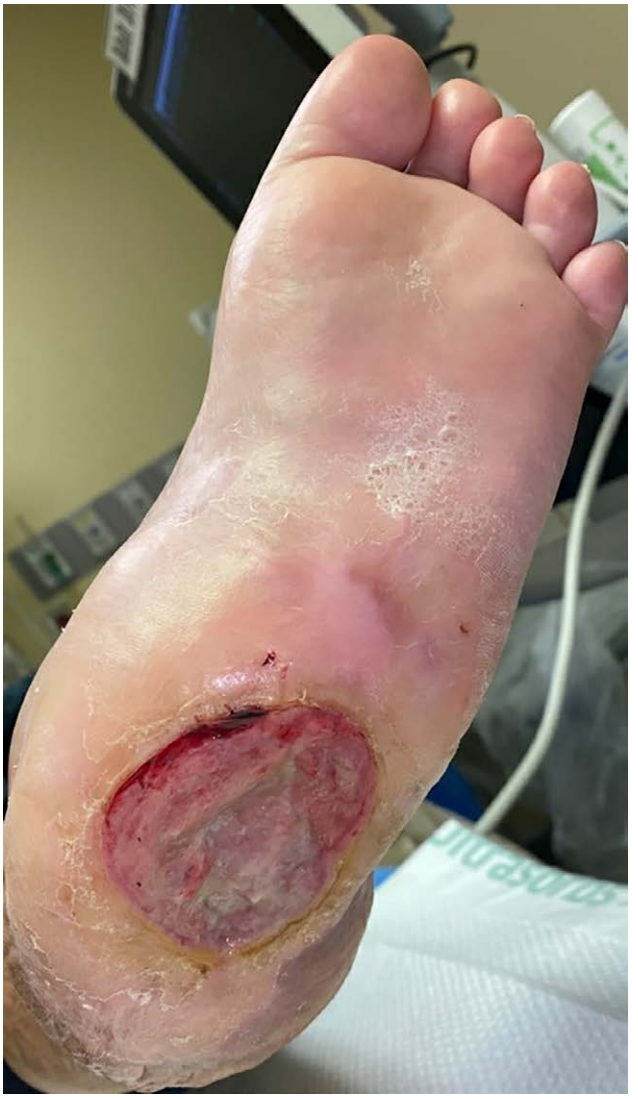

**Fig. 2.** Wound displaying granulation tissue following placement of the SHSFM.

Postamputation, the heel region including calcaneal bone and regenerated tissue was sent to a central laboratory and processed into H&E-stained slides with the patient's consent. Assessment of the slides was performed at the treating institution by a board-certified pathologist. Six sections were taken from the specimen down to and including the calcaneus. Newly granulated tissue was assessed at the superficial, middle, and deep wound bed, as well as at the bone and tissue interface. Tissue assessment was preformed using semiqualitative methods (Table 1). Institutional review board approval was not needed for a single histopathology analysis. The principles outlined in the Declaration of Helsinki were followed.

## RESULTS

Pathologist examination of the H&E-stained slides revealed less than 1 mm epithelium ingrowth beyond the

**Table 1. Pathology Scoring Guide Used for Assessment of Slides at Superficial, Middle, and Deep Wound Bed, and Bone and Tissue Interface**

| | |
|---|---|
| **Inflammatory Response (Neutrophils, Eosinophils, Lymphocytes, Plasma Cells, Macrophages, and Multinucleated Giant Cells)** | |
| 0 | 0 or absent |
| 1 | Rare, 1–5/hpf (giant cells = 1–2/hpf) |
| 2 | 5–10/hpf (giant cells = 3–5/hpf). |
| 3 | Moderate, heavy infiltrates |
| 4 | Packed (giant cells = sheets) |
| Nature of newly deposited collagen (collagen maturation) within the wound site | |
| 0 | No collagen deposition |
| 1 | Scanty collagen deposition as loose, poorly organized stroma |
| 2 | More notable collagen deposition than score 1, majority of stroma still loose, poorly organized with collagen fibers predominantly oriented parallel and perpendicular to skin surface |
| 3 | More notable collagen deposition than score 2, majority of stroma dense, organized with collagen fibers oriented parallel to the skin surface |
| Amount of epithelialization at the wound edges | |
| 0 | No ingrowth of epithelium beyond wound edge |
| 1 | Less than 1 mm of ingrowth of epithelium beyond wound edge on one or both sides of wound |
| 2 | Greater than 1 mm of ingrowth of epithelium beyond wound edges on both sides of the wound but not fully reepithelialised |
| 3 | Wound surface is completely covered by epithelium |
| Approximation of the extent of viable granulation tissue filling the wound bed | |
| 0 | No granulation tissue filling wound |
| 1 | ~1%–25% of the wound bed filled |
| 2 | ~25%- 50% of the wound bed filled |
| 3 | ~50%–75% of the wound bed filled |
| 4 | ~75%–100% of the wound bed filled |
| 5 | >100% of the wound bed filled (excessive granulation tissue) |
| Vascularization with the wound bed | |
| 0 | Absent |
| 1 | Very few small vessels scattered throughout the wound bed |
| 2 | Numerous blood vessels in few areas with mostly low numbers of blood vessels throughout the wound bed |
| 3 | Moderate, numerous blood vessels interspersed throughout portions of the wound bed with areas of lower vascular density interspersed throughout |
| 4 | Marked, numerous blood vessels interspersed through the wound bed |
| Presence of foreign material or bacteria | |
| P | Present |
| A | Absent |
| Evidence of osteomyelitis in observed bone | |
| P | Present |
| A | Absent |

hpf, high- power field.

wound edge, as well as mild acute inflammation and collagen formation. Approximately 75% of the wound depth was filled with viable granulation tissue. Examination of the deep wound bed revealed moderate new vascularization and moderate collagen deposition. The majority of stroma was dense and organized with collagen fibers oriented parallel to the skin surface (Fig. 3). At the interface of granulation tissue formation over bone, there was no evidence of necrosis or bacterial colonization, and osteomyelitis had resolved. Mild inflammation was observed, as determined by the number of inflammatory cells present within the sample, ranging from five to 10 within the high power field.

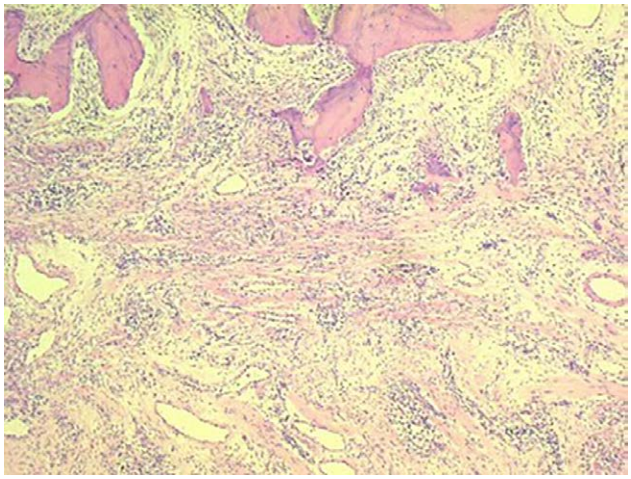

**Fig. 3.** Deep section of the bed under treated wound demonstrating increased vascularization and organizing collagen deposition.

## DISCUSSION

Excellent granulation tissue developed over an exposed, periosteum-devoid calcaneal bone after use of SHSFM, despite failure with other advanced therapies. Improved plantar sensibility was also reported by the patient. Pathologic assessment revealed minimal inflammatory response, notable collagen deposition, increased vascularization, and resolution of osteomyelitis.

The synthetic, engineered design of the SHSFM likely contributed to the clinical and histologic results observed. The SHSFM resembles ECM through electrospun polymers, and therefore does not undergo decellularization processes, which may alter ECM structure. Additionally, the SHSFM's resorption rate matches tissue ingrowth and typically resorbs in 1–3 weeks.[5] Prior histologic studies have demonstrated that more slowly degrading bioscaffolds elicit more chronic inflammation and poorly organized fibrous tissue formation, compared with organized collagen deposition and mild inflammation observed here.[7]

Xenogeneic dermal regenerative templates have demonstrated increased inflammation when high bacterial counts are present.[8] Presently, mild inflammation was observed with no evidence of bacteria or osteomyelitis. The degradation byproducts of the SHSFM are known to elicit a mildly acidic microenvironment which is unsuitable for many bacterial strains.[5,9]

The SHSFM eliminates tissue tracking time and cost, and demonstrates rapid granulation tissue formation with less inflammation than biologic modalities.[5] However, the widespread use of SHSFM is currently limited by the lack of outpatient coverage by private insurers.

This histopathological analysis serves to highlight potential uses of SHSFM in complex wounds with exposed structures. Considering the uniqueness of this wound,

outcomes are difficult to generalize or to compare with similar cases. The positive clinical and histopathological results observed warrant further investigation.

## CONCLUSIONS

This analysis demonstrates the SHSFM's ability to encourage granulation tissue formation over exposed, devitalized bone in a challenging clinical location. Histopathological assessment of newly formed tissue demonstrated minimal inflammatory response, neovascularization, and resolved osteomyelitis within a chronically exposed bone.

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## DISCLOSURES

*Dr. MacKay receives consulting fees from Axogen, Integra LifeSciences, and Trimed.*

*Texas Tech Health Sciences has received research support from Acera Surgical Inc. MacEwan and Sallade both declare employment and stock options from Acera Surgical, Inc.*

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